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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/914,190	03/20/2002	Keizaburo Miki	0760-0294P	9592

2292 7590 08/29/2003

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EXAMINER
BERTOGLIO, VALARIE E

ART UNIT	PAPER NUMBER
1632	10

DATE MAILED: 08/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/914,190	MIKI ET AL.	
	Examiner	Art Unit	
	Valarie Bertoglio	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Response to Amendment

Applicant's arguments filed 05/08/2003, paper number 9, have been fully considered but are not persuasive. Claims 1-5 have been cancelled. Claims 6 and 8 have been amended. Claims 9-17 have been added. Claims 6-17 are pending and under consideration in the instant action.

Claim Rejections - 35 USC § 112-1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 8,9 and 11-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

The claimed invention as a whole is not adequately described if the claims require essential or critical elements that are not adequately described in the specification and that is not conventional in the art as of applicants effective filing date. Possession may be shown by actual

reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641,1646 (1998).

In the instant case the claimed "substitutes which relate to pigment formation" encompassed by the claim lack a written description. The specification fails to describe what substitutes fall into this genus and it was unknown as of Applicants' effective filing date what substitutes would have the property of "relating to pigment formation". The specification describes only that genes relating to coloring include pigments and enzymes that participate in pigment-formation reactions (page 3, paragraph 1). The specification does not describe any attributes of a "substitute" which relates to pigment formation and has not provided a correlation between the structures of known reporter genes or pigment genes and a the structure of a "substitute". There is no evidence on the record of a relationship between the structures of any substitutes relating to pigment formation and the structures of genes relating to coloring described in the specification on pages 3, paragraph 1, that would provide any reliable information about the structure of substitutes which relate to pigment formation encompassed by the claim.

In view of the above considerations one of skill in the art would not recognize that applicant was in possession of the necessary common features or attributes possessed by any member of the genus substitutes which relate to pigment formation. Therefore, only the genes relating to coloring described in the specification on page 3 paragraph 1, but not the full breadth of the claims meet the written description provision of 35 U.S.C. §112, first paragraph.

University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that "to fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention".

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Amended claims 6-8 and newly added claims 9-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The previous rejection is applicable to claims 6-17 for the reasons of record advanced on pages 2-6 of the previous office action mailed 12/04/2002 and are reiterated below.

1) The rejection is on the basis that the specification does not enable making a transgenic mollusk that secretes a colored protein into the pearl. The purpose of the invention is to make a colored pearl (refer to the specification, page 2, lines 20-22 and previous office action, page 3, 1st paragraph). The specification teaches expressing a GFP transgene in the mantle of a mollusk (page 11, lines 8-23; page 12, lines 15-27). However, the specification does not teach that GFP is secreted from the mantle, which is necessary to obtain a colored pearl.

The rejection is also based on the lack of guidance in the specification describing how to make the transgenes used in generating the transgenic mollusks of the invention. Teachings in the specification use a GFP fusion transgene where GFP is operably linked to either the prism protein or the mantle protein (page 11, lines 8-23; page 12, lines 15-27). The specification fails

to provide enough information to determine the structure of the fusion genes. It is not clear where the linker was ligated, what coding sequences or secretion signals from the prism or mantle proteins were included, or how the fragments were "hybridized to obtain a fusion gene". These teachings are not adequate to obtain GFP expression in the mantle and secretion into a pearl using a GFP transgene fusion. As stated in the previous office action, mailed 12/04/2002, the state of the art of generating transgenic mollusks was that the phenotype resulting from any given transgene is unpredictable (refer to pages 3-4 of the previous office action). Thus, in order for one of skill in the art to make the claimed mollusk, appropriate and detailed guidance as to the structure of the transgenes used is necessary to overcome the unpredictability in the art. Therefore, the specification does not provide adequate guidance for one of skill in the art at the time the invention was made to overcome the unpredictability set forth by the art, as described in the previous office action, to obtain the phenotype of interest, i.e. to obtain secretion of a color producing gene product into the pearl of a transgenic mollusk.

In addressing the rejection on the basis that the specification does not demonstrate secretion of the transgene product into the pearl and does not adequately describe the transgenes used, Applicants argue that the claims have been amended to be commensurate with the disclosed invention. Applicants add claim 10, which narrows the scope of the gene encoded by the transgene to a fluorescent protein. This argument is not persuasive as it does not address the rejection and its relevance to the rejection is unclear. The rejection is based on the failure to demonstrate that the colorant is secreted from the mantle such that it is incorporated into the pearl. Applicants also argue that the elements of the present invention are adequately described in the specification on pages 3 and on page 5, line 13-page 6, line 6. The description on these

pages fails to provide adequate detail for one of skill in the art to generate the claimed mollusks such that the unpredictability of phenotype inherent in generating transgenic mollusks is overcome. The specification does not describe the detailed structure of the transgenes, in particular, how to fuse the genes with the appropriate linker sequences such that the transgene is expressed to the appropriate levels and is secreted from the mantle and incorporated into the pearl.

2) The rejection is on the basis that the specification does not enable making and using all transgenic mollusks to secrete a colored protein in making a colored pearl is maintained (see previous office action, mailed 12/04/2002, page 5, 2nd paragraph). The transgenic mollusks claimed are used for generating a colored pearl (page 2, lines 20-22; page 14, lines 14-15). However, not all mollusks, such as shrimp, snails, lobsters, octopus et al., generate pearls. Therefore, claims 6-17 should be limited to transgenic, pearl-producing mollusks such as Bivalvia or abalone.

Applicants failed to respond to the rejection and thus, this aspect of the rejection is maintained.

3) The specification fails to enable making the transgenic mollusks of claims 14 and 17.

Claim 14 encompasses transgenic mollusks comprising a transgene encoding a fusion protein wherein the fusion protein comprises a foreign gene fused to another gene selected from the group consisting of nacreous layer protein gene, prism layer skeleton protein gene and calcium carbonate-crystallizing enzyme. The specification teaches fusing a foreign gene (GFP) to the prism protein gene (page 11, line 8-page 12, line 1) and the mantle protein gene (page 12, line15-page 13, line 9). The specification does not teach a fusion gene comprising the nacreous

layer protein gene, the prism layer skeleton protein gene or the calcium carbonate-crystallizing enzyme. It is not stated that the prism layer skeleton protein gene is the same gene as the prism protein gene.

Claim 17 encompasses a transgenic mollusk comprising a recombinant vector comprising a promoter wherein the promoter is the actin gene promoter or a heat shock promoter. The specification teaches the use of adenoviral promoters (page 6, line 26-page 7, line 12; page 12, lines 19-27)) or mollusk prism protein promoter (page 11, lines 11-16). The specification does not teach using the actin gene promoter or a heat shock promoter.

The state of the art at the time of filing held that the phenotype of transgenic mollusks comprising various transgene constructs is unpredictable (see previous office action mailed 12/04/2002, pages 3-4). Specifically, the level of activity from various promoters and the length of time the transgene remained active was not predictable. The specification does not teach how to fuse a foreign gene to the nacreous layer protein gene, the prism layer skeleton protein gene or the calcium carbonate-crystallizing enzyme such that the foreign protein is produced in the mantle. The specification does not teach how to make a transgenic mollusk comprising a transgene comprising the actin gene promoter or a heat shock promoter such that the transgene is expressed in the mantle. Moreover, the specification fails to provide guidance that correlated expression of a fusion gene in the mantle of a mollusk with secretion of a colored pearl. The specification teaches expression of a transgene in the mantle but does not teach that the transgene product is secreted from the mantle, is incorporated into the pearl or that the pearl is fluorescent as a result of expression of the transgene in the mantle. Because the claims are directed to fusion proteins with various promoters and because the specification fails to provide guidance as to the

activity of the promoter/fusion constructs in transgenic mollusks, it would require undue experimentation for one of skill in the art at the time of filing to determine whether the transgenes encompassed by the claims would be expressed appropriately in the mantle to generate a colored pearl. Therefore, the rejection is maintained for the reasons of record and as discussed in the previous paragraphs.

Claim Rejections - 35 USC § 112-2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Amended claims 6-8 and newly added claims 9 and 11-17 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicant(s) regard as their invention. Applicants' arguments to the rejection set forth on pages 6-8 of the previous office action mailed 12/04/2002 have been fully considered and are partially persuasive.

1) Claims 6-8 and newly added claim 9 are indefinite because the metes and bounds of what applicants consider "desired" cannot be determined.

Applicant argues that the indefiniteness rejections are regarding claims 1-5, which have been cancelled, and thus rendering the rejection moot. This argument is not persuasive because the rejection also applies to pending claims 6-9. Thus, the rejection is maintained.

2) Claims 6, 8, and 9 are indefinite as written. The claims are directed to methods of producing a transgenic mollusk of either claim 10 or 11 and embrace use of a desired gene. Claims 10 or 11 are directed to transgenic mollusks that require a gene that encodes a fluorescent protein. The claims are indefinite because it appears practice of claims 6, 8, and 9 would not

result in production of the transgenic mollusks of claims 10 or 11. Claims 7 depends from claim 6 and is thus included in this rejection. Appropriate correction is required.

3) Newly added claim 9 is unclear as written. The phrase "...microinjecting into gonad of male and/or female of mollusk a recombinant vector into which a desired foreign gene to be introduced" is unclear. It is not clear whether the 'desired foreign gene' is to be introduced into the recombinant vector or into the gonad. Appropriate correction is required.

4) Claim 10 is indefinite as written. The claim is directed to foreign genes that encode substances which relate to pigment formation the expression of which results in emission of fluorescence. The specification has defined substances which relate to pigment formation as those substances that catalyze a reaction resulting in pigment formation (such as, for example, β-galactosidase). Fluorescent proteins, which result in emission of fluorescence appear to be different from substances that relate to pigment formation given the definitions provided by the instant specification and the prior art. Accordingly, it appears that the instant specification has not provided a definition for a substance relating to pigment formation, the expression of which results in emission of fluorescence. Appropriate correction is required. Claims 6-7, 9, 12-14 and 17 depend from claim 10.

5) Newly added claim 11 is unclear as written. The phrase "...comprising a recombinant vector comprising a nucleic acid construct and a promoter that is operably linked to a foreign gene..." can be interpreted that the "nucleic acid construct" is separate and distinct from "a promoter that is operably linked to a foreign gene". If the nucleic acid is separate from the promoter that is operably linked to a foreign gene, the fluorescence (line 5) does not relate back

to the foreign gene, but relates back to the nucleic acid construct. Appropriate correction is required. Claims 12-17 depend from claim 11 and are thus included in this rejection.

6) The term "substitutes" renders newly added claim 11 unclear. It is not clear in the claim and is not described in the specification what a "substitute" encompasses. Both the meaning and the metes and bounds of the term "substitutes" are unclear. Claims 12-17 depend from claim 11 and are thus included in this rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1) Applicants arguments pertaining to the rejection of claims 1-4 and 8 under 35 U.S.C. 102(b) as being anticipated by Burns (USPN 5,969,211) have been fully considered and are persuasive. Claims 1-4 have been cancelled rendering the rejection of these claims moot. Claim 8 has been amended to depend from newly added claim 11, which adds limitations that the transgene product results in emission of fluorescence in the mantle tissue of the mollusk. Burns did not teach transgenic mollusks comprising a transgene wherein the transgene encoded a fluorescent product or wherein the transgene was expressed in the mantle. The rejection of claims 1-4 and 8 under 35 U.S.C 102 (b) as being anticipated by Burns has been withdrawn.

2) Applicants arguments pertaining to the rejection of claims 1-3 and 8 under 35 U.S.C. 102(b) as being anticipated by Raynter (PCT/US95/14685) have been fully considered and are

persuasive for the reasons stated in the preceding paragraph. Raynter did not teach transgenic mollusks comprising a transgene wherein the transgene encoded a fluorescent product or wherein the transgene was expressed in the mantle. The rejection of claims 1-3 and 8 under 35 U.S.C 102 (b) as being anticipated by Raynter has been withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1) Applicants arguments pertaining to the rejection of claims 1-5 and 8 under 35 U.S.C. 103(a) as being unpatentable over Burns (USPN 5,969,211) in view of Godwin (*PNAS,* 1998, vol. 95, pp. 13042-13047) have been fully considered and are persuasive. Claims 1-5 have been cancelled rendering the rejection of these claims moot. Claim 8 has been amended to depend from newly added claim 11, which adds limitations that the transgene product is expressed in the mantle tissue of the mollusk. Neither Burns nor Godwin taught or suggested transgenic mollusks comprising a transgene wherein the transgene is expressed in the mantle. The rejection of claims 1-5 and 8 under 35 U.S.C 103 (a) as being unpatentable over Burns in view of Godwin has been withdrawn.

2) Applicants arguments pertaining to the rejection of claims 1-5 and 8 under 35 U.S.C. 103(a) as being unpatentable over Raynter (PCT/US95/14695) in view of Godwin (*PNAS,* 1998, vol. 95, pp. 13042-13047) and Burns (USPN 5,969,211) have been fully considered and are persuasive. Claims 1-5 have been cancelled rendering the rejection of these claims moot. Claim 8

has been amended to depend from newly added claim 11, which adds limitations that the transgene product is expressed in the mantle tissue of the mollusk. Neither Raynter nor Godwin nor Burns taught or suggested transgenic mollusks comprising a transgene wherein the transgene is expressed in the mantle. The rejection of claims 1-8 under 35 U.S.C 103 (a) as being unpatentable over Raynter in view of Godwin and Burns has been withdrawn.

3) Applicants arguments pertaining to the rejection of claims 1-8 under 35 U.S.C. 103(a) as being unpatentable over Burns (USPN 5,969,211) in view of Ogawa (*1995, Journal of Reproduction*, Vol. 41, pages 379-382) have been fully considered and are persuasive.

Claims 1-5 have been cancelled rendering the rejection of these claims moot. Claims 6-8 have been amended to depend from newly added claim 11, which adds limitations that the transgene product is expressed in the mantle tissue of the mollusk. Neither Burns nor Ogawa taught or suggested transgenic mollusks comprising a transgene wherein the transgene is expressed in the mantle. The rejection of claims 1-8 under 35 U.S.C 103 (a) as being unpatentable over Burns in view of Ogawa has been withdrawn.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is 703-305-5469. The examiner can normally be reached on Mon-Weds 6:00-2:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds can be reached on 703-305-4051. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234.

Valarie Bertoglio
Examiner
Art Unit 1632

Deborah Reynolds
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